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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/024,654	12/17/2001	Frank W.R. Chaplen	245-61614	3259

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KLARQUIST SPARKMAN, LLP
One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, OR 97204

EXAMINER
DAVIS, RUTH A

ART UNIT	PAPER NUMBER
1651	10

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/024,654	CHAPLEN ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *16-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 25-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1 – 6 in Paper No. 9 is acknowledged. The traversal is on the grounds that the inventions are related and that examiner has not provided adequate reasons for the inventions' distinctness. This is not found persuasive because as stated in the previous office action, the inventions above are independent and distinct, each from the other because they have acquired a separate status in the art as a separate subject for inventive effect and require independent searches (as indicated by the different classification). The search for each of the above inventions is not co-extensive particularly with regard to the literature search. Further, a reference which would anticipate the invention of one group would not necessarily anticipate or even make obvious another group.

However, upon entry of the amendment filed February 24, 2003, claims 1 – 15 and 25 – 27 will be examined together as a single group. The inventions of groups V – VII remain subject to restriction from the elected group.

The requirement is still deemed proper and is therefore made FINAL.

Claims 16 – 24 have been withdrawn as being drawn to non-elected subject matter, claims 1 – 15 and 25 – 27 have been considered on the merits.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1 – 15 and 25 – 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and its dependents are drawn to a method for detecting bioactive compounds, however are rendered vague and indefinite because the method does not set forth any steps that positively identifies when a bioactive compound is detected. The mere recitation of "detecting a change" is not sufficient to accomplish the claimed detecting method. Moreover, it is unclear how one would practice the method of detecting, by detecting.

Claim 1 and its dependents are further indefinite because it is unclear what type of change is required to positively detect the bioactive compound.

Claim 5 is confusing because it is unclear how a bacteria, fungus, virus, plant or animal is a compound.

In claim 7, line 1, "The method of identifying" lacks sufficient antecedent basis.

Claim 7 and its dependents are vague and indefinite for reciting "a sample" because it is unclear what the sample is from. For example, is it a sample of a potential bioactive compound or a sample of anything?

Claim 7 and its dependents are further indefinite because it is unclear what response must be detected in order to identify a particular class of compounds.

Claim 10 is rendered vague and indefinite for reciting "a sample" because it is unclear what the sample is from. For example, is it a sample of a potential bioactive compound or a sample of anything?

Claim 10 is further indefinite because it is unclear what response must be detected in order to determine if the sample (or compound) is a calcium channel blocker. Moreover, it is unclear how one would determine if the sample (or compound) is a calcium channel blocker by simply exposing it to erythrophores and melanophores.

Claim 11 and its dependents are confusing because the phrase "color classes of chromatophores" is not adequately defined. It is unclear what applicant intends to include or exclude from the phrase.

The phrase "in functional contact" is confusing because it is unclear what the phrase intends to encompass.

Claim 11 and its dependents are vague and indefinite because it is unclear what and how the color response must be measured to detect if the compound is bioactive or not. Moreover it is unclear how merely measuring a color response detects a bioactive compound.

In claim 12, line 2, "the test compound" lacks sufficient antecedent basis.

Claim 12 is confusing because it is unclear if the chromatophores and compounds are encapsulated together or separately.

In claim 13, line 1, "the test sample" lacks sufficient antecedent basis.

Claim 13 is rendered vague and indefinite because it is unclear what, if any, color response is required to determine the compound bioactive.

Claim 14 is vague and confusing because it is unclear what applicant intends to convey by the phrase "selecting a functional target". Is such a target already known, or is the selecting step additional to the method?

Claim 25 and its dependents are generally vague and indefinite because applicant fails to define "a test cell"; applicant fails to define what constitutes a "control response" by which to select a control compound; applicant fails to define what evaluation must occur in each of the responses such that a detection of a bioactive compound may occur; and it is unclear what compound/combination is being exposed to what such that responses can be measured, observed, and/or evaluated.

Claim 26 is indefinite because it is unclear what cell-induced response is required to be associated with the bacteria to satisfy the required inhibition of chromatophores.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1 – 5, 11 and 25 – 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Elving (US 4985353).

Applicant claims a method for detecting bioactive compounds, the method comprising exposing chromatophores to the compound and detecting a change in at least one chromatophore

in response to the bioactive compound. The detecting step is an optical change in at least one chromatophore; the chromatophores are from fish; the changes are selected from pigment aggregation, dispersion or hue changes; the compound is selected from neurotransmitter, adrenergic agonists, adrenergic antagonists, seratonergic antagonists, hormones, cytoskeletal inhibitors, camp signal transduction modulators, calcium ion signal transduction modulators, membrane voltage, regulators, neurotoxins, protein kinase modulators, caustic irritants, heavy metals, polyaromatic hydrocarbons, organo phosphate nerve agents, psychogenic agents, antihistamines, enzyme inhibitors, algal toxins, bacteria and bacterial protein toxins; or the compound includes a bacteria, fungus, virus, plant or animal.

Elving teaches a method for detecting a pertussis toxin (bioactive compound), comprising exposing toxin sensitive fish chromatophores to a sample (compound), and observing for changes in color (abstract). Specifically, the method includes observing for pigment aggregation and hue changes (col.2 line 36-40). Fish chromatophores are exposed compounds that aggregate pigments, then to samples of body fluid (which contain bacterium) wherein the toxin inhibits pigment aggregation (or the chromatophore response), and is observed for color changes (col.2 line 36-46). Melanophores are used because they provide distinct and rapid color change (col.3 line 1-3) and noradrenaline (norepinephrine) is used as the control (col.3 line 65 – col.4 line 5).

The reference anticipates the claimed subject matter.

6. Claims 1 – 4, 11 and 25 – 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Lerner et al. (US 5462856).

Applicant claims a method for detecting bioactive compounds, the method comprising exposing chromatophores to the compound and detecting a change in at least one chromatophore in response to the bioactive compound. The detecting step is an optical change in at least one chromatophore; the chromatophores are from fish; the changes are selected from pigment aggregation, dispersion or hue changes; the compound is selected from neurotransmitter, adrenergic agonists, adrenergic antagonists, seratonergic antagonists, hormones, cytoskeletal inhibitors, camp signal transduction modulators, calcium ion signal transduction modulators, membrane voltage, regulators, neurotoxins, protein kinase modulators, caustic irritants, heavy metals, polyaromatic hydrocarbons, organo phosphate nerve agents, psychogenic agents, antihistamines, enzyme inhibitors, algal toxins, bacteria and bacterial protein toxins.

Lerner teaches methods for identifying GPC receptors (bioactive compounds/adrenergic agonists and antagonists) wherein melanophores (col.10 line 61) are exposed to a control compound that disperses/aggregates pigments within the melanophores; followed by exposure to the bioactive compound; and determining/detecting any change in pigment dispersion (col.3 line 49-67). Lerner teaches that the pigment cells may be chromatophores, melanophores, or erythrophores (col.3 line 18-21) obtainable from Pisces, or fish (coll3 line 23-26).

The reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1 – 9, 11 and 25 – 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elving and/or Lerner.

Applicant claims a method for detecting bioactive compounds, the method comprising exposing chromatophores to the compound and detecting a change in at least one chromatophore in response to the bioactive compound. The detection is an optical change in at least one chromatophore; the chromatophores are fish, and the changes are selected from pigment aggregation, dispersion or hue changes; the compound is selected from neurotransmitter, adrenergic agonists, adrenergic antagonists, seratonergic antagonists, hormones, cytoskeletal inhibitors, camp signal transduction modulators, calcium ion signal transduction modulators, membrane voltage, regulators, neurotoxins, protein kinase modulators, caustic irritants, heavy metals, polyaromatic hydrocarbons, organo phosphate nerve agents, psychogenic agents, antihistamines, enzyme inhibitors, algal toxins, bacteria and bacterial protein toxins; or the

compound includes a bacteria, fungus, virus, plant or animal; and the chromatophores are Betta chromatophores. The method further comprises exposing a first type of chromatophore to the compound, exposing a second type of chromatophore to the compound, and identifying a class of compounds based on the detected response of the chromatophores, wherein the first and second chromatophores are melanophores and erythrophores from fish; and placing one or more color classes of chromatophores in functional contact with the compound and measuring a color response of at least one of the classes. Alternatively, the method comprises selecting a test cell which produces a cell induced response on the chromatophore, exposing the chromatophore-cell combination to the compound, exposing the chromatophore-cell combination to a control compound, measuring the response of the chromatophore to the control, evaluating the compound based on the cell induced response, the measured response, and the control response; wherein the test cell is a bacteria associated with a cell induced response which inhibits a chromatophore response and the control is norepinephrine.

Elving teaches a method for detecting a pertussis toxin (bioactive compound), comprising exposing toxin sensitive fish chromatophores to a sample (compound), and observing for changes in color (abstract). Specifically, the method includes observing for pigment aggregation and hue changes (col.2 line 36-40). Fish chromatophores are exposed compounds that aggregate pigments, then to samples of body fluid (which contain bacterium) wherein the toxin inhibits pigment aggregation (or the chromatophore response), and is observed for color changes (col.2 line 36-46). Melanophores are used because they provide distinct and rapid color change (col.3 line 1-3) and noradrenaline (norepinephrine) is used as the control (col.3 line 65 – col.4 line 5).

Lerner teaches methods for identifying GPC receptors (bioactive compounds/adrenergic agonists and antagonists) wherein melanophores (col.10 line 61) are exposed to a control compound that disperses/aggregates pigments within the melanophores; followed by exposure to the bioactive compound; and determining/detecting any change in pigment dispersion (col.3 line 49-67). Lerner teaches that the pigment cells may be chromatophores, melanophores, or erythrophores (col.3 line 18-21) obtainable from Pisces, or fish (coll3 line 23-26).

The references do not teach the method wherein both erythrophores and melanophores are used together. However, Lerner specifically teaches that melanophores and/or erythrophores may be used in the methods. At the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use either or both of the named chromatophores in the methods of Lerner and/or Elving with a reasonable expectation for successfully detecting bioactive compounds.

The references do not teach the methods wherein the chromatophores of Betta. However, at the time of the claimed invention, it was well known in the art that Betta have chromatophores. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by common knowledge to practice the methods of Elving and/or Lerner with a reasonable expectation for successfully detecting bioactive compounds.

10. Claims 1 – 4, 6 – 11 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lerner in view of Kotz (1994).

Applicant claims a method for detecting bioactive compounds, the method comprising exposing chromatophores to the compound and detecting a change in at least one chromatophore

in response to the bioactive compound. The detecting step is an optical change in at least one chromatophore; the chromatophores are fish, and the changes are selected from pigment aggregation, dispersion or hue changes; the compound is selected from neurotransmitter, adrenergic agonists, adrenergic antagonists, seratonergic antagonists, hormones, cytoskeletal inhibitors, camp signal transduction modulators, calcium ion signal transduction modulators, membrane voltage, regulators, neurotoxins, protein kinase modulators, caustic irritants, heavy metals, polyaromatic hydrocarbons, organo phosphate nerve agents, psychogenic agents, antihistamines, enzyme inhibitors, algal toxins, bacteria and bacterial protein toxins; and the chromatophores are Betta chromatophores. The method comprises exposing a first type of chromatophore to the compound, exposing a second type of chromatophore to the compound, and identifying a class of compounds based on the detected response of the chromatophores wherein the first and second chromatophores are melanophores and erythrophores, specifically fish chromatophores. The method is useful for identifying calcium channel blockers, comprising exposing an erythrophore to a compound to produce a response, exposing a melanophore to the compound to produce a response, determining if the compound has a calcium channel blocker based on the responses. The method further comprises placing one or more color classes of chromatophores in functional contact with the compound and measuring a color response of at least one of the classes. Alternatively, the method comprises selecting a test cell which produces a cell induced response on the chromatophore, exposing the chromatophore-cell combination to the compound, exposing the chromatophore-cell combination to a control compound, measuring the response of the chromatophore to the control, evaluating the compound based on the cell induced response, the measured response, and the control response.

Lerner teaches methods for identifying GPC receptors (bioactive compounds/adrenergic agonists and antagonists) wherein melanophores (col.10 line 61) are exposed to a control compound that disperses/aggregates pigments within the melanophores; followed by exposure to the bioactive compound; and determining/detecting any change in pigment dispersion (col.3 line 49-67). Lerner teaches that the pigment cells may be chromatophores, melanophores, or erythrophores (col.3 line 18-21) obtainable from Pisces, or fish (coll3 line 23-26).

Lerner does not teach the method wherein both erythrophores and melanophores are used together. However, Lerner specifically teaches that melanophores and/or erythrophores may be used in the methods. At the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use either or both of the named chromatophores in the methods of Lerner with a reasonable expectation for successfully detecting bioactive compounds.

Lerner does not teach the methods wherein the chromatophores of Betta. However, at the time of the claimed invention, it was well known in the art that Betta have chromatophores. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by common knowledge to practice the methods of Lerner with a reasonable expectation for successfully detecting bioactive compounds.

Lerner does not teach the method wherein both erythrophores and melanophores are used to identify calcium channel blockers. However, Kotz teaches erythrophores exhibit pigment aggregation in response to calcium influx whereas melanophores do not (abstract). At the time of the claimed invention, one of ordinary skill in the art would have been motivated by Kotz to

practice the methods of Lerner in order to identify calcium channel blockers because of the known responses between the chromatophores and calcium.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-0196. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ruth A. Davis; rad
May 15, 2003

LEON B. LANKFORD, JR.
PRIMARY EXAMINER